The amendment to claim 1, which restricts the genus "allergy symptoms not associated with respiratory congestion" to the group consisting of headache, irritated eyes and lethargy, is supported by the specification. Specifically, this group of symptoms are disclosed in Examples XXXI, XXXII, and XXXIII on page 18 of the specification. The amendment to claim 8, which restricted the genus "asthma symptoms not associated with respiratory congestion" to the symptom constriction of airways are fully supported. Specifically, the smooth muscle caused constriction of airways is well-known by one of ordinary skill to be a symptom of asthma (See Gerald W. Staton and Roland H. Ingram, Medicine, Ch. 4, Sec. II (David C. Dale, ed., Web MD) (2001)), and a patent need not teach, and preferably omits, what is well known in the art. See *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

A copy of the amendments made herein with markings to show changes made is provided as Appendix A. Also, a copy of the pending claims after amendments is provided as Appendix B.

II. The Outstanding Rejections

Claims 1-7 stand rejected under 35 U.S.C. §112 (first paragraph) for failing to enable treatment of allergy symptoms not associated with respiratory congestion in a patient via any route of administration.

Claims 8-14 stand rejected under 35 U.S.C. §112 (first paragraph) for failing to enable treatment of asthma symptoms not associated with respiratory congestion in a patient via any route of administration.

Claims 1-15 and 20 stand rejected under 35 U.S.C. §112 (second paragraph) for being indefinite; claims 1-7 because "the allergy symptoms not associated with respiratory congestion" lacks antecedent basis; claim 8 because the phrase "not associated with respiratory

congestion" is indefinite; and claim 20 because the claim fails to further limit claim 15 from which it depends.

Claims 1-7 stand rejected under 35 U.S.C. §103(a) as being unpatentable over McMichael, U.S. Patent No. 6,100,244 ('244 Patent); McMichael, U.S. Patent No. 5,955,442 ('442 Patent); McMichael, U.S. Patent No. 5,726,160 ('160 Patent); and McMichael, U.S. Patent No. 6,096,721 ('721 Patent) in view of Kuby (Immunology, Kuby ed., page 360 (1992)).

Claims 1-7 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of '422 Patent or claims 1-7 of '160 Patent in view of Kuby (Immunology, Kuby ed., page 360 (1992)).

Claims 8-14 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of '422 Patent or claims 1-7 of '160 Patent in view of Murray (The Textbook of Respiratory Medicine, (1988)).

III. Patentability Arguments

A. The Rejections of Claims 1-7 Under 35 U.S.C. §112 (First Paragraph) Should Be Withdrawn.

The rejections of claims 1-7 under 35 U.S.C. §112 (first paragraph) for failing to enable treatment of allergy symptoms not associated with respiratory congestion should be withdrawn because the claims have been amended to recite specific allergy symptoms of headache, irritated eyes, and lethargy, which are the allergy symptoms not associated with respiratory congestion of the present invention that Applicants' specification teaches treatment of. In addition, the rejection of claims 1 and 3-6 for failing to enable treatment via any route of administration should be withdrawn as amended claims are now directed to treatment via sublingual administration.

The disclosure in Applicants' specification teaches treatment of allergy symptoms not associated with respiratory congestion, particularly in Examples XXXI, XXXII, and XXXIII on pages 18-19, which teach the treatment of the allergy symptoms of headache, irritated eyes, and lethargy. In Example XXXI, the patient displayed the allergy symptoms "headache, irritated eyes and lethargy" (page 18, lines 7-9) and upon DNA treatment of the present invention the results were "complete relief lasting for at least sixty minutes" (page 18, lines 9-11). In Example XXXII, the patient displayed the allergy symptoms "headache, scratching of eyes" (page 18, lines 16-19) and the DNA treatment of the present invention "counters such symptoms" (page 18, lines 19-21). In Example XXXIII, the patient displayed the allergy symptoms "headache, watery eyes and weakness" (page 18, lines 24-27) and the DNA treatment of the present invention "results in a decrease or elimination of symptoms within 15-20 minutes" page 18, line 27 - page 19, line 2). Additionally, these examples are working examples and not prophetic as confirmed by the McMichael Declaration and Applicants request specific explanation under MPEP §716.01 as to why this evidence is insufficient.

These particular allergy symptoms, headache, irritated eyes and lethargy, are not known in the art to be associated with respiratory congestion. Congestion is understood in the art to mean the presence of abnormal amount of fluid in the vessels or passages of a part or organ. Stedman's Medical Dictionary, 26th ed., Marjory Sprayear, Ed., William & Wilkins, Baltimore, MD, p. 382 (1995). In the case of respiratory congestion, the part or organ are those of the respiratory system, which is defined in Stedman's Medical Dictionary, p. 1753, as the air passages from the nose to the pulmonary aveoli. An association between symptoms requires some functional connection between such symptoms. Stedman's Medical Dictionary, p. 157. The presence of abnormal amounts of fluid or phlegm in the air passages would not be understood by one of ordinary skill to be functionally connected to headache, irritated eyes, and

lethargy. Instead, one of ordinary skill would associate allergy symptoms such as dyspnea, coughing, rhinitis, and anaphylactic shock with respiratory congestion because all of these symptoms are understood in the art to be functionally related to respiratory congestion.

While Applicants maintain that the specification enables treatment by multiple modes of administration, the claims have been amended to recite only sublingual administration in order to expedite allowance.

Accordingly, the rejection of claims 1-7 under 35 U.S.C. §112 (first paragraph) should be withdrawn.

B. The Rejections of Claims 8-14 Under 35 U.S.C. §112 (First Paragraph) Should Be Withdrawn.

The rejections of asthma treatment claims 8-14 under 35 U.S.C. §112 (first paragraph) as failing to enable treatment of symptoms in an asthma patient should be withdrawn because the claims have now been amended to recite the asthma symptom of constriction of airways which is not associated with respiratory congestion.

Those of ordinary skill in the art of pulmonary disease understand that asthma is characterized by smooth muscle caused constriction of the bronchial airways which lead to difficulty in breathing. In particular, asthma is characterized by hypertrophy and hyperplasia of airway smooth muscle. Gerald W. Staton and Roland H. Ingram, Medicine, Ch. 4, Sec. II, p. 2. While the Patent Office cites Murray, The Textbook of Respiratory Medicine, for the fact that mucus plugs are present in patients who die from severe asthma, which are relatively few cases, Murray confirms that "mucous gland hyperplasia and increased numbers of goblet cells are unusual in patients with severe asthma."

The claimed treatment of the asthma symptom of constriction of airways not associated with respiratory congestion is further supported by the facts provided in the

Declaration of John McMichael (paragraph 3) filed along with the April 20, 2001 Amendment and Response. The McMichael Declaration states that the practice of the method of the invention was successful in alleviating the constriction of airways of two subjects (subjects in Examples XXXIV and XXXV) in a manner which allowed them to carry out the activities of daily life. As evidence that these results were not the product of clearance of respiratory congestion, the Declaration states that beneficial results were unaccompanied by a productive cough, which normally expels the congestion causing sputum.

While Applicants maintain that the specification enables treatment by multiple modes of administration, the claims have been amended to recite only sublingual administration in order to expedite allowance.

Accordingly, claims 8-14 are fully enabled and the rejections of claims 8-14 under 35 U.S.C. §112 (first paragraph) should be withdrawn.

C. The Rejection of Claims 1-15 and 20 Under 35 U.S.C. §112 (Second Paragraph) Should Be Withdrawn.

The rejection of claims 1-7 under 35 U.S.C. §112 (second paragraph) for indefiniteness and lack of antecedent basis should be withdrawn because the claims have been amended to recite the specific symptoms of headache, irritated eyes and lethargy that are symptoms not associated with respiratory congestion.

The rejection of claims 8-14 under 35 U.S.C. §112 (second paragraph) for indefiniteness and lack of antecedent basis should be withdrawn because the claims have been amended to further recite that the particular symptom not associated with respiratory congestion is "constriction of airways."

Furthermore the claims have also been amended to provide proper antecedent basis for the phrase "the allergy symptoms not associated with respiratory congestion." In

addition, claim 20 has been canceled; therefore the basis for rejecting claims 15 and 20 under this section is removed. Accordingly, the rejections of claims 1-15 and 20 under 35 U.S.C. §112 (second paragraph) should now be withdrawn.

D. The Rejection of Claims 1-7 Under 35 U.S.C. §103(a) Should Be Withdrawn.

The rejection of claims 1-7 under 35 U.S.C. §103(a) over '244 Patent, '442 Patent, '160 Patent, and '721 Patent in view of Kuby should be withdrawn because the cited references, combined or alone, fail to render obvious the claimed method for treating allergy symptoms headache, irritated eyes and lethargy, because the cited references suggest or teach the relief of respiratory congestion but not the symptoms headache, irritated eyes and lethargy, which are not associated with respiratory congestion.

The present application claims the use of DNA compositions disclosed therein to treat the allergy symptoms headache, irritated eyes and lethargy, which are not associated with respiratory congestion unlike the symptoms treated in the cited art. The '244, '442, '721, and '160 Patents disclose methods of treating respiratory illness comprising administration of DNA, specifically to treat respiratory congestion, but do not teach treatment of the symptoms headache, irritated eyes and lethargy, which are not associated with respiratory congestion. The methods of the cited art work by helping to reduce viscosity of the mucus in the respiratory tract by reducing mucus production, thinning mucus, or producing a productive cough. Additionally, the '244 and '721 Patents disclose another aspect of the method of treating respiratory illness, the method comprising treating symptoms of respiratory distress not associated with aberrant mucous accumulation. The disclosed respiratory illnesses with this characteristic do not include headache, irritated eyes and lethargy. Accordingly, none of the cited references disclose the treatment of the particular allergy symptoms headache, irritated eyes and lethargy, nor do the

references suggest that treatment of respiratory congestion could be useful for such non-respiratory congestion symptoms.

The disclosure in Kuby fails to add any teaching or suggestion that would render the present invention obvious. Kuby simply discloses anaphylaxis, a class of allergic reactions, which is associated with hay fever. Symptoms can include watery exudation of the conjunctivae, nasal mucosa, and upper respiratory tract as well as sneezing and coughing. There is no disclosure about using treatments for respiratory congestion in order to treat the allergy symptoms headache, irritated eyes and lethargy, which are not associated with respiratory congestion.

Applicants' amended claims 1-6 are not directed to symptoms associated with respiratory congestion or obstruction of airways, but are directed to the allergy symptoms of headache, irritated eyes, and lethargy, which the prior art fails to teach or suggest. Accordingly, the rejection of claims 1-7 under 35 U.S.C. §103(a) over the '244, '442, '160, and '721 Patents in view of Kuby should be withdrawn.

E. The Double Patenting Rejection of Claims 1-7 Should Be Withdrawn.

The double patenting rejection of claims 1-7 over claims 1-6 of '442 Patent or claims 1-7 of '160 Patent in view of Kuby should be withdrawn because the claims of the cited patents in view of Kuby do not render current claims 1-7 obvious because those claims are directed to methods of relieving respiratory congestion whereas current claims 1-7 are directed to methods of treating allergy symptoms **not** associated with respiratory congestion, those symptoms being headache, irritated eyes, and lethargy. Although allergy patients may have respiratory congestion, there is no teaching in the prior art that suggests successful treatment of

the non-congestion symptoms of allergies, headache, irritated eyes and lethargy, using a treatment for respiratory congestion.

One of ordinary skill would not know that the allergy symptoms headache, irritated eyes, and lethargy, which are symptoms **not** associated with respiratory congestion, could be successfully treated with the claimed methods of the '442 and '160 Patents, which are directed towards relieving respiratory congestion. Accordingly, the obviousness-type double patenting rejection of claims 1-7 should be withdrawn.

F. The Double Patenting Rejection of Claims 8-14 Should Be Withdrawn.

The double patenting rejection of claims 8-14 over claims 1-6 of '442 or claims 1-7 of '160 in view of Murray should be withdraw since Applicants have filed a Terminal Disclaimer over the '442 and '160 Patents, submitted herewith.

CONCLUSION

For all of the foregoing reasons, the rejections should now be withdrawn and allowance of all pending claims 1-6, 8-13, and 15-19 is respectfully solicited. Should the Examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, he is invited to contact the undersigned attorney at the number indicated below.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN
6300 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606-6402
(312) 474-6300

November 5, 2001

By: _____
Jeffrey S. Sharp
Reg. No. 31,879

APPENDIX A

VERSION WITH MARKING TO SHOW CHANGES MADE

In the Specification:

Please amend the specification as follows.

Please replace the paragraph on page 1, starting on line 3 with the following paragraph:

--This application is a continuation-in-part of U.S. Patent Application Serial No. 09/432,948 filed November 3, 1999, issued August 8, 2000 as U.S. Patent No. 6,100,244, which is a continuation-in-part of U.S. Patent Application Serial No. 09/037,895 filed March 10, 1998, issued August 1, 2000 as U.S. Patent No. 6,096,721, which is a continuation-in-part of U.S. Patent Application Serial No. 08/755,092 filed November 22, 1996, issued March 10, 1998 as U.S. Patent No. 5,726,160 which is a continuation of U.S. Patent Application Serial No. 08/421,232 filed April 13, 1995.--

Please replace the paragraph on page 14, starting on line 9 with the following paragraph:

--According to this example, a five year old female presented with severe recurrent otitis media in the right ear with bulging of the tympanic membrane. The subject was treated with sublingual administration of one drop of DNA (0.0006 mg/drop) four times daily for seven days. When the subject was rechecked two days later the mother reported the child's temperament and energy improved the first evening. She went to school the next day. On exam, she had an [injected] infected tympanic membrane, but the bulging was gone. Significantly, this subject has been treated for OM numerous times in the past with antibiotics.-

In the Claims:

Please cancel claim 7, 14, and 20.

1. [AMENDED TWICE] A method for treating allergy symptoms not associated with respiratory congestion selected from the group consisting of headache, irritated eyes and lethargy in a patient, comprising the step of:

administering through a sublingual route in a manner so as not to effect gene transfer an effective amount of DNA in a pharmaceutically-acceptable vehicle to a patient having allergy symptoms such that the allergy symptoms not associated with respiratory congestion selected from the group consisting of headache, irritated eyes and lethargy are reduced.

8. [AMENDED TWICE] A method for treating the asthma symptom[s] of constriction of airways which is not associated with respiratory congestion in a patient, comprising the steps of:

administering in a manner so as not to effect gene transfer a therapeutically effective amount of DNA in a pharmaceutically-acceptable vehicle to a patient having the asthma symptom[s such that the asthma symptoms] of constriction of airways which is not associated with respiratory congestion [are]is reduced.

APPENDIX B

PENDING CLAIMS AFTER AMENDMENT

1. A method for treating allergy symptoms not associated with respiratory congestion selected from the group consisting of headache, irritated eyes and lethargy in a patient, comprising the step of:

administering through a sublingual route in a manner so as not to effect gene transfer an effective amount of DNA in a pharmaceutically-acceptable vehicle to a patient having allergy symptoms such that the allergy symptoms not associated with respiratory congestion selected from the group consisting of headache, irritated eyes and lethargy are reduced.

2. The method according to claim 1 wherein said DNA is administered sublingually in the form of a liquid drop.

3. The method according to claim 1 wherein said vehicle is selected from the group consisting of water, saline, albumin, or dextrose.

4. The method according to claim 1 wherein said effective amount of DNA is from about 0.00012 mg to about 0.003 mg DNA.

5. The method according to claim 1 wherein said effective amount of DNA is about 0.0006 mg of DNA.

6. The method according to claim 1 wherein said patient is a human.

8. A method for treating the asthma symptom of constriction of airways which is not associated with respiratory congestion in a patient, comprising the steps of:

administering in a manner so as not to effect gene transfer a therapeutically effective amount of DNA in a pharmaceutically-acceptable vehicle to a patient having the asthma symptom of constriction of airways which is not associated with respiratory congestion is reduced.

9. The method according to claim 8 wherein said DNA is administered sublingually in the form of a liquid drop.

10. The method according to claim 8 wherein said vehicle is selected from the group consisting of water, saline, albumin, or dextrose.

11. The method according to claim 8 wherein said effective amount of DNA is from about 0.00012 mg to about 0.003 mg DNA.

12. The method according to claim 8 wherein said effective amount of DNA is about 0.0006 mg of DNA.

13. The method according to claim 8 wherein said patient is a human.

15. A method for treating symptoms of otitis media, comprising the step of:

administering eardrops to the ear in a manner so as not to effect gene transfer an effective amount of DNA in a pharmaceutically-acceptable vehicle to a patient having otitis media such that pain symptoms associated with otitis media are reduced.

16. The method according to claim 15 wherein said vehicle is selected from the group consisting of water, saline, albumin, or dextrose.

17. The method according to claim 15 wherein said effective amount of DNA is from about 0.00012 mg to about 0.003 mg DNA.

18. The method according to claim 15 wherein said effective amount of DNA is about 0.0006 mg of DNA.

19. The method according to claim 15 wherein said patient is a human.